Lapatinib Side-Effect Management

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Lapatinib is an oral dual tyrosine kinase inhibitor targeting epidermal growth factor receptor and HER2. Diarrhea and dermatologic adverse events are reported commonly by patients treated with lapatinib. Diarrhea can range from mild to severe based on the agents used in combination with lapatinib. The adverse events may diminish quality of life, reduce treatment adherence, and lead to discontinuation of therapy. Consequently, proactive management of diarrhea is crucial, especially in patients receiving lapatinib in combination with other agents that also cause diarrhea. As the utility of lapatinib expands, crucial proactive diarrhea-management and dose-reduction strategies are evolving to decrease the likelihood of grade 3 or 4 toxicity. With regard to dermatologic adverse events, most are mild to moderate in severity, are of limited duration, and frequently do not require treatment intervention. However, in some patients, management of dermatologic adverse events is of great importance. This article reviews data regarding diarrhea and dermatologic adverse events in patients treated with lapatinib and summarizes the key role that oncology nurses play in educating patients about the potential for adverse events and the importance of preventive measures, ongoing surveillance, appropriate treatment, and dose reductions.

The development of therapies targeting epidermal growth factor receptor (EGFR) family members has resulted in adverse events that require new management strategies. Lapatinib (Tykerb®/Tyverb®, GlaxoSmithKline) is an orally active dual tyrosine kinase inhibitor targeting both EGFR and HER2. Lapatinib is approved in combination with capecitabine for the treatment of HER2-positive metastatic breast cancer that has progressed on a taxane, an anthracycline, and trastuzumab (GlaxoSmithKline, 2008). In a pivotal phase III study, treatment of patients with HER2-positive disease who had previously received a trastuzumab-containing regimen with lapatinib plus capecitabine resulted in a 43% improvement in time to disease progression compared with capecitabine monotherapy ($p < 0.001$), and a trend existed toward improved survival (Cameron et al., 2008; Geyer et al., 2006). Lapatinib also is being investigated as neoadjuvant and adjuvant therapy for breast cancer, as well as for the treatment of a variety of other solid tumors (Fields et al., 2005; Ravaud et al., 2006; Ross et al., 2005; Wülfing et al., 2005).

Lapatinib has been administered to almost 9,000 patients in clinical studies. The most frequently reported adverse events are gastrointestinal disorders (e.g., diarrhea, nausea, vomiting) and dermatologic disorders (e.g., rash, hand-foot syndrome, dry skin) (GlaxoSmithKline, 2008). The adverse events generally are not life threatening; however, failure to adequately manage the events may diminish quality of life, decrease treatment adherence, and potentially result in treatment discontinuation. Proactive education, intense surveillance, and early intervention by oncology nurses in the management of diarrhea are required to maintain quality of life and treatment adherence. This article reviews diarrhea and dermatologic adverse events in patients treated with lapatinib who participated in a number of completed clinical studies in the metastatic setting and two studies in the adjuvant setting. The severity of the events was graded on a scale of 1–4 using the National Cancer Institute Common Toxicity Criteria (v.2.0) and the National Cancer Institute Common Terminology Criteria for Adverse Events (v.3.0) (National Cancer Institute, 1999, 2006). In addition, this article

At a Glance

- Diarrhea and dermatologic adverse events are among the most common toxicities in patients treated with lapatinib alone or in combination.
- Most diarrhea and dermatologic adverse events in patients treated with lapatinib are mild to moderate in severity, are of limited duration, and do not require treatment interruption.
- Proactive management of diarrhea is crucial, especially in patients receiving lapatinib in combination with other agents that also cause diarrhea.

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